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| EXAMINER | |
|---|---|
| DUFFY, BRADLEY | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/770,726 | BROWN ET AL. | |
| | Examiner | Art Unit | |
| | BRADLEY DUFFY | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,5-7 and 26-30* is/are pending in the application.

4a) Of the above claim(s) *30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibits E and F*.

## DETAILED ACTION

### *PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNINTENTIONALLY UNDER 37 CFR 1.137(b)*

1. As set forth in the decision mailed July 22, 2008, the petition has been granted.

### *Continued Examination Under 37 CFR 1.114*

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 22, 2008, has been entered.

3. The amendment filed January 22, 2008, is acknowledged and has been entered. Claims 1 and 5 have been amended.

4. Claims 1, 5-7 and 26-30 are pending in the application. Claim 30 has been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. The restriction requirement in the reply filed November 22, 2006, was treated as an election without traverse (MPEP § 818.03(a)).

5. Claim 1, 5-7 and 26-29 are under examination.

6. The following Office action contains NEW GROUNDS of rejection and objection.

***Election/Restriction***

7. The amendment filed January 22, 2008, amends claims 1, 5-7 and 26-29, so as to be directed in the alternative to an invention that is independent or distinct from the invention originally claimed. Furthermore, due to this amendment claim 30 is now clearly directed to an invention that is independent or distinct from the invention originally elected. These claims are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

In this case, claim 1 has been amended to be drawn to methods that detect a nucleic acid comprising SEQ ID NO:31.

In contrast, the claims in the originally elected invention are drawn to methods for detecting nucleic acids of the NEK2, PLK1, ATR and CHEK1 genes. However, as set forth in the Office action mailed February 20, 2007, at page 6, the specification does not identify a "PLK1" gene. Therefore, while the specification identifies NEK2, ATR and CHEK1 as genes with cDNA sequences of SEQ ID NO:26, SEQ ID NO:1 and SEQ ID NO:12, respectively, and are therefore drawn to the elected invention, SEQ ID NO:31 is not identified as a nucleic acid sequence for any of the originally elected NEK2, PLK1, ATR and CHEK1 genes in the specification. Accordingly, methods of detecting a nucleic acid comprising SEQ ID NO:31 are drawn to an invention independent or distinct from the invention originally elected and examined.

Furthermore, there would be a serious burden to consider the amended claims drawn to detecting a nucleic acid comprising SEQ ID NO:31. For example, this amendment would require a sequence search of SEQ ID NO:31 in up to eight different databases and detailed and extensive consideration of the results by the Examiner. Accordingly, the search of the claims as drawn to the methods of detecting a nucleic acid comprising SEQ ID NO:31 would require undue burden due to the extensive searching and review that would be required, in addition to the consideration of different patentability issues.

Notably, while Applicant presented a new claim 30 in the amendment filed May 21, 2007, drawn to the method of claim 1, wherein the sequence is SEQ ID NO:31,

because "the sequence is SEQ ID NO:31" lacked antecedent basis in the previous claim 1, it appeared that claim 30 was intended to be part of the elected invention as it was drawn to the method of claim 1 that was only drawn to the elected invention. However, as explained in the previous Office action at page 3, the lack of antecedent basis precluded the examination of the claim for compliance with the requirements set forth under 35 U.S.C. §§ 112, first paragraph, 102, and 103. Accordingly, it is now proper to withdraw claim 30 from further consideration because the amendment to claim 1 makes claim 30 now clearly drawn to subject matter independent or distinct form the originally elected invention and because the amendment would now cause serious and undue burden to search and examine for compliance with the requirements set forth under 35 U.S.C. §§ 112, first paragraph, 102, and 103, which have not previously been searched or considered.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 30 is withdrawn from consideration as being directed to a nonelected invention and claims 1, 5-7 and 26-29 are withdrawn to the extent they read on methods of detecting a nucleic acid comprising SEQ ID NO:31 as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Applicant is further reminded that applicant cannot, as a matter of right, file a request for continued examination (RCE) to obtain continued examination on the basis of claims which are drawn to an invention other than the one elected (see MPEP § 819 and 821.03).

***Priority***

8. With regards to the issue of priority, Applicant has argued that the amendment to claim 1 has enabled the claimed invention and submits that the effective filing date should be February 4, 2003, because the claims are now in compliance with 35 U.S.C. § 112, first paragraph.

In response, this argument is not found persuasive because the claims remain rejected under 35 U.S.C. § 112, first paragraph, for the reasons detailed below.

To receive benefit of the earlier filing date under 35 USC §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Accordingly, the effective filing date of claims 1, 5-7 and 26-29 is deemed the filing date of the instant application, namely February 4, 2004.

***Grounds of Objection and Rejection Withdrawn***

9. Unless specifically reiterated below, Applicant's amendment and/or arguments filed January 22, 2008, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed August 22, 2007.

***New Grounds of Objection***

***Claim Objections***

10. Claims 1, 5-7 and 26-29 are objected to as being drawn in the alternative to the subject matter of a non-elected invention (i.e., methods of detecting the nucleic acid with the nucleic acid sequence of SEQ ID NO:31).

***Grounds of Objection Maintained***

11. The objection to Claim 7 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is maintained. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

In this case, Applicant has argued at page 9 of the response filed January 22, 2008, that the amendment to claim 1 to recite "corresponding normal lung or colon tissue" has obviated this objection without further explanation.

In response, it remains unclear how (or whether) the limitation recited in claim 7 further limits the subject matter of claim 1. Since claim 1 is presented in the alternative, the objection is maintained because the subject matter of the method of claim 1 encompasses detecting an expression profile of at least one nucleic acid in a *lung* cancer tissue, as opposed to a colon cancer tissue, from a human subject having colon cancer in accordance with claim 7, and therefore, it is unclear how, or whether the limitation recited in claim 7 further limits the subject matter of claim 1.

Must the subject have both colon and lung cancers?

12. The objection to Claim 26 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is maintained. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

In this case, Applicant has argued at page 9 of the response filed January 22, 2008, that the amendment to claim 1 to recite "corresponding normal lung or colon tissue" has obviated this objection without further explanation.

In response, it remains unclear how (or whether) the limitation recited in claim 26 further limits the subject matter of claim 1. Since claim 1 is presented in the alternative, the objection is maintained because the subject matter of the method of claim 1 encompasses detecting an expression profile of at least one nucleic acid in a *colon*

cancer tissue, as opposed to a lung cancer tissue, from a human subject having lung cancer in accordance with claim 26, and therefore, it is unclear how, or whether the limitation recited in claim 26 further limits the subject matter of claim 1.

Must the subject have both colon and lung cancers?

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1, 5-7 and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 5-7 and 26-29 are indefinite in the recitation of "corresponding normal lung or colon tissue". In this case, Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2008 by Merriam-Webster, Inc.), which is available on the Internet at <http://www.m-w.com/>, defines the term "correspond" as "to be equivalent or parallel" and it is unclear how normal lung tissue might be considered equivalent or parallel to colon cancer tissue or how normal colon tissue might be considered equivalent or parallel to lung cancer tissue. As currently presented, the claims encompass methods of comparing e.g., a normal lung tissue reference profile that somehow corresponds to an expression profile from colon cancer tissue. How does normal lung tissue correspond to colon cancer tissue? Does it correspond by being from the same person, correspond because both tissues comprise cells or do the tissues correspond in some other fashion? The metes and bounds of the claims cannot be unambiguously interpreted for these reasons.

Accordingly, the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

If Applicant views the invention as a method wherein a colon cancer tissue expression profile is compared to a normal colon tissue reference expression profile, and in the alternative as a method wherein a lung cancer tissue expression profile is compared to a normal lung tissue reference expression profile, then the Examiner suggests writing such methods as separate independent claims because such independent claims would delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1, 5-7 and 26-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

In this case, claim 1 has been amended to recite methods comprising the steps of: a) detecting an expression profile of at least one nucleic acid in a colon or lung cancer tissue from a human subject, wherein said at least one nucleic acid comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 12, and SEQ ID NO:26; b) comparing said expression profile to a "corresponding normal lung or colon tissue reference expression profile" of said at least one nucleic acid; and determining whether the nucleic acid is overexpressed compared to the corresponding normal lung or colon tissue reference expression profile, thereby to detect a marker of the colon or lung cancer. Accordingly the claims encompass methods comprising the steps of: a) detecting an expression profile of at least one nucleic acid in a **lung** cancer tissue from a human subject, wherein said at least one nucleic acid comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 12, and SEQ ID NO:26; b) comparing said expression profile to a corresponding normal **colon** tissue reference expression profile of said at least one nucleic acid; and determining whether the nucleic acid is overexpressed compared to the corresponding **colon** tissue reference expression profile or methods comprising the steps of: a) detecting an expression profile of at least one nucleic acid in a **colon** cancer tissue from a human subject, wherein said at least one nucleic acid comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 12, and SEQ ID NO:26; b) comparing said expression profile to a corresponding normal **lung** tissue reference expression profile of said at least one nucleic acid; and determining whether the nucleic acid is overexpressed compared to the corresponding normal **lung** tissue reference expression profile which, as will be explained in further detail, do not appear to have adequate written support in the specification as originally filed.

At page 9 of the response filed January 22, 2008, Applicant has indicated that support for this amendment can be found throughout the specification, for example, at pages 9-11, 14, 15 , 18, 19, 23, and 30-32.

Contrary to Applicant's assertion, however, it does not appear that the specification, including the claims, as originally filed, provides written support for the language of the claims.

In this case, after careful review of the specification, as filed, it does not appear that the original disclosure supports methods of comparing lung cancer expression profiles to corresponding normal colon tissue reference profiles or methods of comparing colon cancer expression profiles to corresponding normal lung tissue reference profiles which are broadly, but reasonably encompassed by the amended claims which results from the ambiguity in the alternative recitation of "corresponding normal lung or colon tissue" as detailed in the above rejection of the claims under 35 U.S.C. § 112, second paragraph. Notably, in Table 6A starting at page 113, the specification compares gene expression in colon cancer tissue to normal colon tissue or compares gene expression in lung cancer tissue to normal lung tissue in order to establish that the nucleic acids with the nucleic acid sequence of SEQ ID NO: 1, SEQ ID NO: 12, and SEQ ID NO:26 are overexpressed in colon cancer tissue as compared to normal colon tissue or are overexpressed in lung cancer tissue as compared to normal lung tissue. However, support for comparing colon cancer tissue to normal lung tissue or for comparing lung cancer tissue to normal colon tissue, as broadly, but reasonably encompassed by the claims, could not be found in the specification as originally filed. Accordingly, it is not immediately apparent that one of skill in the art would recognize that Applicant originally contemplated such methods as part of the invention based on the specification as originally filed. Therefore, for these reasons, it is submitted that Applicant's amendment has introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

Given the apparent difference in the breadth of the claims and that of the pertinent disclosures it is submitted that this clearly illustrates that such amendments have in fact introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. §112, first paragraph.

Otherwise this issue might be resolved if Applicant were to point to other disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary written support for the language of the instant claims.

***Grounds of Rejection Maintained***

***Claim Rejections - 35 USC § 112***

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. The rejection of claims 1, 5-7 and 26-29 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a method of detecting colon adenocarcinoma markers comprising detecting an expression profile of at least one nucleic acid in a colon cancer tissue from a human subject, wherein said at least one nucleic acid is selected from the group of SEQ ID NO:26, SEQ ID NO:1, and SEQ ID NO: 12, wherein said at least one nucleic acid is overexpressed compared to a normal colon tissue reference control, **and while being enabling for using** a method of detecting lung adenocarcinoma markers comprising detecting an expression profile of at least one nucleic acid in a lung cancer tissue from a human subject, wherein said at least one nucleic acid is selected from the group of SEQ ID NO:26, SEQ ID NO:1, and SEQ ID NO: 12, wherein said at least one nucleic acid is overexpressed compared to a normal lung tissue reference control, **and while being enabling for using** any process encompassed by the claims, which has been described by the prior art, **does not reasonably provide enablement for using** the claimed processes, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

At page 8 of the amendment filed January 22, 2008, Applicant has traversed this ground of rejection.

Applicant's arguments traversing the ground of rejection set forth in the preceding Office action have been carefully considered but not found persuasive to obviate this rejection.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

In this case, Applicant has argued that amending the claims to recite "corresponding normal lung or colon tissue" has overcome this rejection.

In response, this argument is not found persuasive because, as explained in the above rejection of the claims under 35 U.S.C. 112, first paragraph, the amended methods broadly, but reasonably encompass methods of comparing lung cancer

expression profiles to corresponding normal colon tissue reference profiles or methods of comparing colon cancer expression profiles to corresponding normal lung tissue reference profiles. However, one of skill in the art would not be reasonably enabled to use such comparison steps because nucleic acid expression in tissues of different origins is highly unpredictable and therefore, it cannot be known if comparing samples from two different tissues would have any use.

Thus, contrary to Applicant's argument, the amendment to claim 1 has not obviated the ground of rejection set forth in the preceding Office action because the amendment does not require that the expression profile of the colon cancer tissue be compared to a normal colon tissue reference expression profile as set forth in the preceding Office action, or, strictly in the alternative, that the expression profile of the lung cancer tissue be compared to a normal lung tissue reference expression profile.

In conclusion, upon careful and complete consideration of Applicant's arguments and after consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation, and this rejection is maintained.

***Claim Rejections - 35 USC § 102***

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

20. The rejection of claims 1, 7, 26 and 29 under 35 U.S.C. 102(a) as being anticipated by WO 03/025138 A2 (Afar et al, published March 2003), is maintained.

In this case, Applicant has argued that Afar is not available as prior art because the instant claims are entitled to a priority date of February 4, 2003.

In response, the currently amended claims are not entitled to a priority date of February 4, 2003, because the claims remain rejected under 35 U.S.C. § 112, first paragraph (see above priority discussion).

Therefore, for the reasons of record as explained in the preceding Office action, Afar still anticipates the instant claims and this rejection is maintained.

***Claim Rejections - 35 USC § 103***

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. The rejection of claims 1, 5, and 6 under 35 U.S.C. 103(a) as being unpatentable over WO 03/025138 A2 (Afar et al, published 2003), is maintained.

In this case, Applicant has argued that Afar is not available as prior art because the instant claims are entitled to a priority date of February 4, 2003.

In response, the currently amended claims are not entitled to a priority date of February 4, 2003, because the claims remain rejected under 35 U.S.C. § 112, first paragraph (see above priority discussion).

Therefore, for the reasons of record as explained in the preceding Office action, the claimed methods would be obvious over the teachings of Afar and this rejection is maintained.

24. The rejection of claims 1, 5-7, 26 and 27 under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,632,936 (Carr, published 2003), in view of US Patent 7,101,985 (Elledge et al, published 2006) and US Patent 6,709,832 (Von Knebel Doebertiz et al, published 2004), is maintained.

In this case, Applicant has argued that Elledge is not available as prior art because the instant claims are entitled to a priority date of February 4, 2003.

In response, the currently amended claims are not entitled to a priority date of February 4, 2003, because the claims remain rejected under 35 U.S.C. § 112, first paragraph (see above priority discussion).

Therefore, for the reasons of record as explained in the preceding Office action, the claimed methods would be obvious over the teachings of Carr, in view of Elledge et al and Von Knebel Doebertiz et al, and this rejection is maintained.

25. The rejection of claims 1, 5-7, 26 and 28 under 35 U.S.C. 103(a) as being unpatentable over US Patent 7,081,340 (Baker et al, published 2006), in view of US Patent 6,709,832 (Von Knebel Doebertiz et al, published 2004), is maintained.

In this case, Applicant has argued that Baker is not available as prior art because the instant claims are entitled to a priority date of February 4, 2003.

In response, the currently amended claims are not entitled to a priority date of February 4, 2003, because the claims remain rejected under 35 U.S.C. § 112, first paragraph (see above priority discussion).

Therefore, for the reasons of record as explained in the preceding Office action, the claimed methods would be obvious over the teachings of Baker et in view of Von Knebel Doebertiz et al, and this rejection is maintained.

***Prior art under 102(e)***

26. In the interest of compact prosecution, because Applicant appears to be arguing that the above references are not available as prior art *if* the instant claims are entitled to a priority date of February 4, 2003, the Examiner notes that the above references are also available as prior art under 102(e) based on their earlier effective filing dates which are all before February 4, 2003. Accordingly, a showing that the prior art is not 102(a) prior art is not sufficient *if* the claims were amended to subject matter entitled to a priority date of February 4, 2003.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 102***

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

28. Claims 1, 7, 26 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/059377 A2 (Mack et al, published 2002).

The claims are herein drawn to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a colon cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal colon tissue to determine whether said nucleic acid is overexpressed in the cancer tissue or to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a lung cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue.

Mack et al teach methods of detecting an expression profile of an mRNA comprising a nucleotide sequence that is 100% identical to the instantly claimed SEQ ID NO:26[1] in a cancer tissue and a normal tissue and that the tissues can be colon tissue or lung tissue which determines whether said nucleic acid is overexpressed in the cancer tissue; see entire document (e.g., attached alignment; pages 29 and 30). Accordingly, it is submitted that Mack et al teach processes that are materially and manipulatively indistinguishable from the instantly recited process. Therefore, absent a showing of any difference, Mack et al anticipate these claims.

29. Claims 1, 7, 26 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by US 20040072154 A1 (Morris et al, effective filing date at least 11/30/01).

The claims are herein drawn to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a colon cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal colon tissue to determine whether said nucleic acid is overexpressed in the cancer tissue or to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a lung cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue.

Morris et al teach methods of detecting an expression profile of an mRNA comprising a nucleotide sequence that is 100% identical to the instantly claimed SEQ ID NO:26[2] in a cancer tissue and a normal tissue and that the tissues can be colon tissue or lung tissue which determines whether said nucleic acid is overexpressed in the cancer tissue; see entire document (e.g., attached alignment; pages 2 and 3). Accordingly, it is submitted that Morris et al teach processes that are materially and manipulatively indistinguishable from the instantly recited process. Therefore, absent a showing of any difference, Morris et al anticipate these claims.

***Claim Rejections - 35 USC § 103***

30. Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/059377 A2 (Mack et al, published 2002).

Claims 1, 5, and 6 are directed to the method of claim 1, wherein the normal tissue reference profile is an average expression profile of said at least one nucleic acid

[1] See the alignment of these sequences attached here as Exhibit E.
[2] See the alignment of these sequences attached here as Exhibit F.

in a plurality of reference biological samples of cancer-free subjects and wherein said expression profiles are determined using RT-PCR or nucleic acid arrays.

Additionally, Mack et al teach said expression profiles being determined using RT-PCR or nucleic acid arrays (e.g., pages 58 and 59).

With regard to claims 5 and 6, it is noted that Mack et al do not expressly teach that the normal tissue reference profile is an "average" expression profile of said nucleic acid from cancer-free subjects. Nevertheless, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to measure the expression profile of said at least one nucleic acid in more than one reference biological sample, and then determine the average value of the expression profiles of that nucleic acid in the samples, so as to compare the expression profile of the nucleic acid in the colon cancer tissue and the average value in cancer-free colon tissue or to compare the expression profile of the nucleic acid in the lung cancer tissue and the average value in cancer-free lung tissue, because it would be recognized that the average value better reflects the standard level of expression in normal, non-cancerous colon or lung tissues, respectively. This is because it would be expected that the normal level of expression of any nucleic acid will vary in normal subjects, at least to some extent, such that the difference in the levels of expression in the colon or lung cancer tissue and any one specimen of the corresponding normal tissue might be more or less significant, which could lead the practitioner of the process to falsely conclude that the nucleic acid is or is not overexpressed in the cancerous tissue. Therefore, one ordinarily skilled in the art at the time the invention was made to would have been motivated to do so in order to more accurately determine whether or not the nucleic acid is overexpressed in the colon cancer tissue relative to the standard level of expression that occurs in the normal colon tissues or in the lung cancer tissue relative to the standard level of expression that occurs in the normal lung tissues, respectively.

Because Mack et al. teaches the expression profiles are determined using RT-PCR or nucleic acid array, it would have been *prima facie* obvious to determine the average value of the expression profiles of that nucleic acid in the normal samples using such methodology. One ordinarily skilled in the art would have been motivated to do so

because such methodology was both routine and conventional at the time the invention was made, and was recognized to be very sensitive.

31. Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20040072154 A1 (Morris et al, effective filing date at least 11/30/01).

Claims 1, 5, and 6 are directed to the method of claim 1, wherein the normal tissue reference profile is an average expression profile of said at least one nucleic acid in a plurality of reference biological samples of cancer-free subjects and wherein said expression profiles are determined using RT-PCR or nucleic acid arrays.

Additionally, Morris et al teach said expression profiles being determined using RT-PCR or nucleic acid arrays (e.g., page 14).

With regard to claims 5 and 6, it is noted that Morris et al do not expressly teach that the normal tissue reference profile is an "average" expression profile of said nucleic acid from cancer-free subjects. Nevertheless, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to measure the expression profile of said at least one nucleic acid in more than one reference biological sample, and then determine the average value of the expression profiles of that nucleic acid in the samples, so as to compare the expression profile of the nucleic acid in the colon cancer tissue and the average value in cancer-free colon tissue or to compare the expression profile of the nucleic acid in the lung cancer tissue and the average value in cancer-free lung tissue, because it would be recognized that the average value better reflects the standard level of expression in normal, non-cancerous colon or lung tissues, respectively. This is because it would be expected that the normal level of expression of any nucleic acid will vary in normal subjects, at least to some extent, such that the difference in the levels of expression in the colon or lung cancer tissue and any one specimen of the corresponding normal tissue might be more or less significant, which could lead the practitioner of the process to falsely conclude that the nucleic acid is or is not overexpressed in the cancerous tissue. Therefore, one ordinarily skilled in the art at the time the invention was made to would have been motivated to do so in order to more accurately determine whether or not the nucleic acid is overexpressed in the colon

cancer tissue relative to the standard level of expression that occurs in the normal colon tissues or in the lung cancer tissue relative to the standard level of expression that occurs in the normal lung tissues, respectively.

Because Morris et al. teaches the expression profiles are determined using RT-PCR or nucleic acid array, it would have been *prima facie* obvious to determine the average value of the expression profiles of that nucleic acid in the normal samples using such methodology. One ordinarily skilled in the art would have been motivated to do so because such methodology was both routine and conventional at the time the invention was made, and was recognized to be very sensitive.

***Conclusion***

32. No claim is allowed.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
August 16, 2008